Atty. Dkt. No. 029318-0109

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Applicant:	Bosch et al.
Title:	DRY POWDER AEROSOLS OF NANOPARTICULATE DRUGS
Appl. No.:	09/190,138
Filing Date:	11/12/1998
Examiner:	James Henry Alstrum Acevedo
Art Unit:	1616
Confirmation Number:	6300

REPLY BRIEF

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Sir:

Under the provisions of 37 C.F.R. § 41.39, Appellants are filing this Reply Brief in response to the Examiner's Answer (the "Answer"), dated May 26, 2006.

I. Introduction

Pursuant to their right under 37 C.F.R. § 41.39, Appellants take this opportunity to respond to certain comments in the Examiner's Answer.

II. Appellants' Remarks Regarding the Examiner's Position

A. The Examiner's Allegation That "Edwards teaches smooth and spherical microparticle drug for inhalation that are aggregates of nanometer particle" is False

In the Examiner's Answer, the Examiner stated that in col. 9, lines 11-21, "Edwards teaches smooth and spherical microparticle drug for inhalation" and that "both the polymers comprising the micron-sized particles taught by Edwards and the therapeutic agents contained therein are obviously nanosized particles because the size of molecules are on the nanometer length scale." Examiner's Answer at 6. Appellants respectfully disagree.

Foremost, the invention in Edwards describes particles for drug delivery that have a mean diameter of between 5 μm and 30 μm, and this feature, in combination with a particular tap density, "yield an aerodynamic diameter of between one and five microns." Edwards at col. 5, lines 10- 13, emphasis added. Indeed, the aerodynamic diameter, according to Edwards, is an essential characteristic of the particles in Edwards because the described diameter provides for maximum particle deposition within the lungs. *Id* at col. 5, lines 10-13.

It is not taught or even suggested, however, that the size of the particles be less than 5 μm diameter, or even be as small as possible. To the contrary, Edwards describes *avoiding* the use of particles less than five microns in diameter since they are subject to phagocytosis. Edwards at col. 5, lines 14-18. Further, Edwards even states that particles having a larger diameter may be selected and still result in equivalent delivery to the lungs if they are aerodynamically light. *Id* at col. 5, lines 18-22.

Moreover, how such larger particles can be made suitable for use in Edwards' invention is also described. In fact, Edwards provides that "[i]mproved delivery can be

obtained by using particles with a rough or uneven surface relative to those with a smooth surface" and that "different properties of the particle which can contribute to the aerodynamic lightness include . . . the presence of irregular surface structure, or pores or cavities within the particle." *Id* at col. 5, lines 22-24 and lines 64-67, respectively. Therefore, not only does Edwards not disclose spherically shaped particles, there would be no motivation to modify Edwards to obtain a spherically shaped particle less than 1 μm, or even a spherically shaped particle of any size. Edwards specifically teaches away from small spherical particles and encourages particles with a "rough or uneven surface" to improve aerodynamic lightness.

B. The Examiner's Allegation That "Edwards teaches crystalline nanoparticulate particles" is False

In the Examiner's Answer, the Examiner stated that Edwards teaches crystalline nanoparticulate particles. Examiner's Answer at 7. Appellants respectfully disagree.

The therapeutic agents of Edwards do not have an effective average particle size of less than 1 μm, as required by the presently pending claims. Edwards specifically states that the particles "have a . . . mean diameter between 5 μm and 30 μm." Edwards at col. 5, lines 10-11. This size characteristic is not trivial and cannot be disregarded. For the obviousness rejection to be proper, the prior art must teach each and every limitation of the claimed invention, including the size feature recited in the claims. And since Edwards (either alone or in combination with another reference) does not teach or suggest a composition comprising spherically shaped aggregates of a nanoparticulate crystalline drug, wherein the drug has an effective average particle size of less than 1 μm, Edwards does not render the claimed invention obvious.

C. The Examiner's Allegation That "Liversidge addresses similar problems raised in Edwards concerning nanosized drug delivery formulations through the respiratory tract" is False

The Examiner stated that Liversidge and Edwards address similar problems and are in the same field of endeavor. Examiner's Answer at 8. Appellants respectfully disagree.

Edwards describes aerodynamically light particles for delivery to the pulmonary system. The particles of Edwards have a larger diameter than prior art particles having sizes

of less than five microns in diameter (Edwards at col. 5, lines 15-17) to avoid phagocytosis. Thus, Edwards is not concerned with (and actively teaches away from) drug particles with an effective average size of less than 1 μm.

In contrast, Liversidge discloses nanosized crystalline drug particles for oral or parenteral administration (but not dry powder aerosol formulations for delivery through the respiratory tract). In other words, Liversidge is concerned with making drug nanoparticles to improve bioavailability during oral and parenteral administration, and Edwards is concerned with making drug particles for inhalation that are larger than 5 μm. In fact, as stated above, Edwards specifically teaches away from making drug particles "less than five microns in diameter, preferably between one and three microns . . ." Thus, Liversidge does not address similar problems raised in Edwards.

In addition, one of skill in the art would not have been motivated to combine the teachings of Edwards and Liversidge since Edwards specifically teaches away from making spherical drug formulations with an effective average particle size of less than 1 μm. Thus, the reference combination does not teach each and every element of the claimed invention.

D. The Examiner's Allegation That "Edwards in view of Dalby or Goodman and Gilman (singly or in combination) teach or suggest spherical nanosized aerosol drug particles" is False

The Examiner stated that the combination of prior art references teach the claimed invention. Examiner's Answer at 9. Appellants respectfully disagree.

As stated above, Edwards does not disclose spherically shaped particle less than 1 μm, or even a spherically shaped particle of any size. Not only are the deficiencies in Edwards not found in the teachings of Dalby or Goodman and Gilman, there would have been no motivation to modify Edwards to obtain the spherically shaped particles claimed in the present invention. Indeed, Edwards encourages a rough particle surface to improve aerodynamic lightness.

III. Conclusion

For all of foregoing reasons, the PTO still has not established a *prima facie* case of obviousness, and the claimed invention is patentable over the cited prior art. Accordingly, Appellants respectfully request the Board to reconsider and reverse the outstanding rejection of the claims.

Respectfully submitted,

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By _____

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